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simultaneously measuring a first change in absorbance of said sample at 450 ± 10 nm and

a second change in absorbance of said sample at 480 ± 10 nm, 546 ± 10 nm, or 575 ± 10 nm; and

determining the difference between the first and second changes in absorbance.

REMARKS

Applicants submit this Reply and Amendment in response to the Examiner's Office Action mailed on November 1, 2002, setting a shortened statutory period for response of three months. In the subject Office Action, the Examiner provisionally rejected claims 12-29 under the judicially created doctrine of obviousness-type double patenting over the claims of copending application number 09/806,983. The Examiner also objected to the specification for informalities, and rejected claims 12-29 under the second paragraph of 35 U.S.C. §112. The Examiner further rejected claims 12-29 under 35 U.S.C. §102(a), claims 16-23 under 35 U.S.C. §102(b), and claims 12-29 under 35 U.S.C. §102(b).

1. Rejection of claims under the judicially created doctrine of obviousness-type double patenting

The Examiner provisionally rejected claims 12-29 over the claims of copending application 09/806,983 (the '983 application) for obviousness-type double patenting. Specifically, the Examiner indicated that claims 12-29 of the present application are not patentably distinct from claims 8-24 of the '983 application. Applicants respectfully traverse this provisional rejection, and assert that the claims of the present and '983 applications define patentably distinct inventions.

These two applications are similar to the extent that both are directed to methods of eliminating interference by hemoglobin in the determination of alkaline phosphatase. The methods of these two applications, however, represent distinctly different approaches to solving the problem of hemoglobin interference.

The claims of the '983 application require a rate-blank measurement, i.e., a monochromatic optical rate measurement at 450 ± 10 nm before adding 4-nitrophenyl phosphate (a rate-blank measurement) and a monochromatic optical rate measurement at 450 ± 10 nm after adding 4-nitrophenyl phosphate (measurement of the main reaction). A secondary wavelength is not required in the methods of the '983 application. The claims of the current application require the use of an optical measurement taken at 450 ± 10 nm in combination with an optical measurement taken at a secondary wavelength, i.e., the methods include a bichromatic optical measurement. In contrast to the methods of the '983 application, the methods of the current application do not utilize a rate-blank measurement.

Furthermore, considering the claims of the '983 application, it would not have been obvious to one of ordinary skill in the art to arrive at the invention defined by the claims of the present application. With the claims of the '983 application in hand, a skilled artisan would not be motivated to produce the invention claimed in the present application because, as indicated in the '983 application, the method of the '983 application produces a complete elimination of interference. Practicing this method, the skilled artisan would have no technological motivation to use other means for eliminating such interference.

Accordingly, the Examiner's provisional rejection of claims 12-29 of the present application should be withdrawn.

2. Objections to the specification for informalities

The Examiner objected to the specification for containing various informalities. Specifically, the Examiner objected to the specification because the various sections are not labeled or separated by headings and the first sentence of Example 1 lacks a period. Applicants have overcome these objections by inserting various heading paragraphs and adding a period to the first sentence of Example 1.

3. Rejection of claims under 35 U.S.C. §112

The Examiner rejected claims 12-29 under the second paragraph of 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicants regard as the invention. Specifically, the Examiner indicated that while the preamble of claims 12 and 28 is directed to a method of eliminating interference, the last step of combining measurements is not seen to perform a function of the preamble.

Applicants respectfully assert that the term "combining" is understood in the art and that the combining step in each independent claim performs a function of the preamble. Applicants respectfully submit that it is known in the art that the term 'combining', as used with optical measurements, means determining the *difference* between two optical measurements. This step contributes to the function of the preamble by achieving the elimination of interference due to hemoglobin.

Applicants have amended all independent claims to more clearly point out the method of the present invention. Specifically, Applicants have amended claims 12, 24 and 28 to distinctly show that the measurements are taken simultaneously and that the last step requires determining the difference between the two measurements.

4. Rejection of claims under 35 U.S.C. §102(a)

The Examiner rejected claims 12-29 under 35 U.S.C. §102(a) as being anticipated by US patent 6,013,467 to Siedel et al. for Blood Substitute Suppression by Peroxides (the '467 patent). The Examiner indicates that the rejection is based on the '467 patent, but also details the relationship between the '467 patent and WO 98/02570 (the Siedel PCT). While the Applicants are willing to use the text of the '467 patent to discuss the rejection to the extent it is identical to the Siedel PCT, they respectfully assert that the rejection cannot be based on the '467 patent as indicated by the Examiner *because the '467 patent is not prior art to the present application*. The Applicants discuss this rejection below as if it had been entered as a rejection based on the Siedel PCT and use the '467 patent simply as an English language version of this reference. Applicants take this approach to facilitate prosecution, and do not thereby make any admission or acknowledgement that the '467 patent constitutes prior art to the claims of the present application.

To properly support a rejection under 35 U.S.C. §102, a reference must disclose each and every limitation of the rejected claim. All independent claims of the present application require first and second optical measurements. The primary measurement is

taken at 450 ±10 nm and the secondary measurement is taken at 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm. The '467 patent does not disclose a primary measurement at 450 ±10 nm with a secondary measurement at 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm and cannot, therefore, properly serve as a rejection under §102.

As indicated by the Examiner, the '467 patent contemplates the use of multiple measurements at different wavelengths (*see* column 2, lines 21-29). However, the only mention of primary and secondary measurements references wavelengths "...of 400-420 nm or/and 520-590 nm where hemoglobin has its main and secondary absorptions." (column 2, lines 25-29). Thus, it is clear that the '467 patent does not disclose the primary measurement wavelength of 450 nm in combination with a secondary wavelength of 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm.

Accordingly, the Examiner's §102 rejection of claims 12-29 based on the Siedel PCT is improper and should be withdrawn.

5. Rejection of claims 16-23 under 35 U.S.C. §102(b)

The Examiner also rejected claims 16-23 under 35 U.S.C. §102(b) as being anticipated by US 6,207,459 to Weisheit et al. for a Method for the Analysis of Medical Samples Containing Haemoglobin (the '459 patent). The Examiner indicates that the rejection is based on the '459 patent, but also details the relationship between the '459 patent and WO 97/45732 (Weisheit PCT I). As with the Siedel et al. reference, the Applicants are willing to use the text of the '459 patent to discuss the rejection to the extent it is identical to Weisheit PCT I. Nevertheless, the rejection cannot be literally based on the '459 patent *because the '459 patent is not prior art to the present application.* The Applicants discuss this rejection below as if it had been entered as a rejection based on Weisheit PCT I and use the '459 patent simply as an English language version of this reference. Applicants take this approach to facilitate prosecution, and do not thereby make any admission or acknowledgement that the '459 patent constitutes prior art to the claims of the present application.

Claims 16-23 all depend from independent claim 12 which requires a primary measurement taken at 450 ±10 nm and a secondary measurement taken at 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm. The '459 patent is devoid of any disclosure of a primary measurement wavelength of 450 nm. It rather discloses a method to *correct* an analyte value measured in a sample containing hemoglobin. This method is very complex, requiring five distinct steps as well as an additional experimental determination of the test specific correction factor. Because the '459 patent does not disclose a measurement taken at a primary wavelength of 450 ±10 nm, this reference cannot properly serve as a basis for rejection under §102.

Accordingly, the Examiner's §102 rejection of claims 16-23 based on Weisheit PCT I is likewise improper and should be withdrawn.

6. Rejection of claims 12-29 under 35 U.S.C. §102(b)

The Examiner rejected claims 16-23 under 35 U.S.C. §102(b) as being anticipated by WO 97/45733 to Weisheit et al. for a Process to Eliminate Hemoglobin Errors When Analyzing Medical Samples (Weisheit PCT II). The Examiner provided an English translation of Weisheit PCT II.

All independent claims of the present application require first and second optical measurements. The primary measurement is taken at 450 ±10 nm and the secondary measurement is taken at 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm. The Weisheit PCT II reference does not disclose a primary measurement at 450 ±10 nm with a secondary measurement at 480 ±10 nm, 546 ± 10 nm, or 575 ± 10 nm and cannot, therefore, properly serve as a rejection under §102.

As indicated by the Examiner, the invention described in Weishet PCT II uses first and second measurements taken at different wavelengths. Also, the secondary wavelength is preferably over 475 ±10 nm (*see* p. 4 of English translation). Weisheit PCT II does not, however, disclose any secondary wavelengths in conjunction with a primary wavelength of 450 ±10 nm, and certainly does not show the claimed wavelengths of 480 ±10 nm, 546 ± 10 nm, and 575 ± 10 nm with a primary wavelength of 450 ±10 nm.

Applicants indeed distinguished Weisheit PCT II in the specification of the current application. Specifically, the applicants indicate that the method of Weisheit PCT II can

> "...only be used for enzymatic UV tests with a main measurement wavelength of 340 nm. Although a complete elimination of Hb interference can be achieved solely by the use of secondary wavelengths 546 or 570 nm, this is not possible for enzymatic chromogenic tests such as the determination of alkaline phosphatase in which the main measurement wavelength is in the range of 415 nm."

(see specification, pages 4-5).

Accordingly, Applicants respectfully request that the Examiner withdraw his rejection of claims 12-29 based on Weisheit PCT II.

CONCLUSION

In light of the above, Applicants have overcome each and every one of the Examiner's objections and rejections. The application is therefore in condition for allowance on the next office action. If, however, the Examiner disagrees and feels that personal communication would facilitate the prosecution of this case, applicants request that the Examiner contact their attorney at the number listed below.

Respectfully submitted,

Dated: April 29, 2003

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Appendix A

Determination according to the recommendation to the Société Francaise de Biologie Clinique according to Ann. Biol. Clin. Vol. 35, 271 (1977).

Appendix B

12. (Amended) A method of eliminating interference by hemoglobin in the determination of alkaline phosphatase in a sample, comprising:

adding 4-nitrophenyl phosphate to said sample;

simultaneously determining a first optical measurement of said sample at 450 ± 10 nm[;] and

[determining] a second optical measurement at one or more secondary wavelengths selected from the group consisting of 480 ± 10 nm, 546 ± 10 nm, and 575 ± 10 nm; and

[combining] determining the difference between the first and second optical measurements.

24. (Amended) A method of determining a level of alkaline phosphatase in a sample containing 4-nitropheny phosphate, the method comprising:

[combining] simultaneously determining a first optical measurement [determined] at 450 ± 10 nm [with] and a second optical measurement [determined] at a secondary wavelength selected from the group consisting of 480 ± 10 nm, 546 ± 10 nm, and 575 ± 10 nm[.]; and

determining the difference between the first and second optical measurements.

28. (Amended) A method of determining a level of alkaline phosphatase in a sample, comprising:

adding 4-nitrophenyl phosphate to said sample;

simultaneously measuring a first change in absorbance of said sample at 450 ± 10 nm[;] and

[measuring] a second change in absorbance of said sample at 480 ± 10 nm, 546 ± 10 nm, or 575 ± 10 nm; and

[combining] determining the difference between the first and second changes in absorbance.